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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Wayne R. Danter

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EXAMINER

RAO, DEEPAK R

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

06/02/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/531,107	Applicant(s) DANTER ET AL.	
	Examiner Deepak Rao	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,5,6,14-27 and 29-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,3,5,6 and 23-27 is/are allowed.
- 6) ☒ Claim(s) 14-18,21,22 and 29 is/are rejected.
- 7) ☒ Claim(s) 19,20,30 and 31 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>20090323</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to the amendment filed on March 23, 2009.

Claims 1, 3, 5-6, 14-27 and 29-31 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

Claims 14-18, 21-22 and new claim 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating breast cancer, lung cancer, colon cancer, ovarian cancer, renal cancer, prostate cancer or leukemia, does not reasonably provide enablement for a method for treatment of cancer involving inappropriate tyrosine kinase activity generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant first argues that 'the claim limits cancer to those involving inappropriate kinase activity'. The specification does not provide sufficient guidance for one of ordinary skill in the art to know what is encompassed by the instant recitation of 'treatment of cancer involving inappropriate tyrosine kinase activity'. The recitation "tyrosine kinase" encompasses all

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members of the protein kinase super family. The state of the art reference of record, Plowman et al., teaches that: "There are several recognized families of cell surface growth factor receptors, including receptor tyrosine kinases (RTKs) ... One of the most abundant classes of receptors are the RTKs, now represented by at least 19 distinct subfamilies. ... Disruptions or imbalances in RTK signaling cascades have been linked to a variety of chronic diseases including cancer and diabetes" (see page 334). The reference further provides that: "Several mechanisms exist to control the specificity of RTK signaling ... Together these factors can dictate whether a given ligand-receptor interaction results in seemingly disparate events such as proliferation or differentiation" (see page 336). As can be seen the reference clearly teaches the diversity and unpredictability involved with the mechanism of tyrosine kinase activity and therefore, one of ordinary skill in the art would have to go through the burden of undue experimentation to use the instantly claimed therapeutic method.

Applicant relies on the test methods described in the specification and the Declaration by Dr. Wayne Danter and argues that 'the specification and declaration show a reasonable correlation to treating cancers associated with inappropriate tyrosine kinase activity'. The 'how to use' portion of the statute has not been addressed sufficiently in the disclosure nor in the Declaration by Dr. Danter. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what diseases and what symptoms are to be treated. The specification combined with the Declaration do not establish enablement for method of treating all types of cancer associated with inappropriate tyrosine kinase activity generally. Applicants have not demonstrated nor have they alleged there

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is any correlation between the *in vitro* assays they disclose in pages 27-29 and clinical efficacy against types of cancers other than those presented in the test data.

As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: “We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.” Case law is clear on this point. In an unpredictable art, such as cancer therapy, *in vitro* assays may be used for enablement only if there is a well-established correlation between the assay and clinical efficacy. *In re Buting*, 163 USPQ 689 establishes that even clinical tests showing that a compound found to be useful in the treatment of two types of cancers was not sufficient for a much broader range.

MPEP 2164.03 provides the relationship of predictability of the art and the enablement requirement (portion of MPEP is provided below for convenience):

2164.03 [R-2] Relationship of Predictability of the Art and the Enablement Requirement

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The “amount of guidance or direction” refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the

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invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification.

In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. See, e.g., *Chiron Corp. v. Genentech Inc.*, 363

F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) (“Nascent technology, however, must be enabled with a specific and useful teaching.” The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee’s instruction. Thus, the public’s end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology.” (citations omitted)).

The “predictability or lack thereof” in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, **if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art.** Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated:

[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof. [Footnote omitted.]

The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, **in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims.** *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). **This is because it is not obvious from the disclosure of one species, what other species will work.**

The instant claims are drawn to ‘a method for treatment of cancer associated with inappropriate tyrosine kinase in a mammal’. The specification does not provide an enabling disclosure for these claims. The testing data provided in the specification at pages 27-29 and the Declaration by Dr. Danter are directed to specific types of cancers and there is insufficient

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guidance how this data is extrapolated to all the methods of use instantly recited. Applicant has not provided how this correlates with the efficacy in treating all types of cancers or other diseases encompassed by the instant methods. Applicant did not state on record or provide any guidance that the assays provided are correlated to the clinical efficacy of the treatment of various disorders encompassed by the claims. As can be seen from specification, the *in vitro* data holds significant role in determining the dosage regimen based on the minimal effective concentration of each of the compound to achieve the desired inhibition of the enzymes.

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

The breadth of applicant's enablement is not commensurate in scope with the claims. Contrary to applicant's arguments, the specification provides little or no guidance to practice the claimed methods. Applicant has not provided sufficient evidence that establishes that the disclosure would have enabled for one skilled in the art at the time of filing. Further, the state of the art does not identify a single class of compounds that can treat all types of diseases or possess the biological activity of the instant claims. Further, one skilled in the art of medicinal therapy recognizes that there are complex interactions between individual genetic, developmental state, sex, dietary, environmental, drug, and lifestyle factors that contribute to the carcinogenic process, making it even more challenging to have a single therapeutic agent for the treatment of diverse diseases. Rigorously planned and executed clinical trials, incorporating measurement of appropriate biomarkers and pharmacodynamic endpoints are critical for selecting the optimal

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dose and schedule. A detailed understanding of the molecular mode of action of the various cytokines, alongside the elucidation of the molecular pathology of individual diseases is required to identify disease types and individual patients that may benefit most from treatment. It is also important to construct a pharmacologic audit trail linking molecular biomarkers and pharmacokinetic and pharmacodynamic parameters to receptor response endpoints. Therefore, it is maintained that applicants have not provided sufficient test assays or data to support the various methods commensurate in scope with the claims, as of the filing date of the application.

Allowable Subject Matter

Claims 1, 3, 5-6, and 23-27 are allowed. Claims 19-20 and 30-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Receipt is acknowledged of the Information Disclosure Statement filed on March 23, 2009 and a copy is enclosed herewith.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**/Deepak Rao/
Primary Examiner
Art Unit 1624**

June 2, 2009